

1. (Three times amended) A method to assess whether a compound first binds to and then enhances the clearing of a cholesterol-containing low density lipoprotein (LDL) after subsequent binding to a low density lipoprotein receptor in a host by increasing the binding affinity of the cholesterol-containing low density lipoprotein to the low density lipoprotein receptor, said method comprising:

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- (a) administering the compound to the host ;
  - (b) isolating the cholesterol-containing low density lipoprotein from the host,
  - (c) determining whether binding has occurred between the compound and the cholesterol-containing low density lipoprotein from the host; thus forming a complex; and
  - (d) determining whether the complex results in a change in the binding affinity of the cholesterol-containing low density lipoprotein to the low density lipoprotein receptor.

2. (Once Amended) The method of claim 1, wherein the compound changes the conformation of apolipoprotein in the cholesterol-containing low density lipoprotein (LDL).

3. (Once Amended) The method of claim 1, wherein the cholesterol-containing low density lipoprotein is very low density lipoprotein (VLDL).

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6. (Three times amended) A method to determine whether a compound first binds to and then increases the clearance of a low density lipoprotein after subsequent binding to a low density lipoprotein receptor in a host by increasing the binding affinity of the low density lipoprotein to the low density lipoprotein receptor, said method comprising

- (i) mixing the compound with the low density lipoprotein;
  - (ii) determining whether the compound binds to the low density lipoprotein and forms a complex; and
  - (iii) determining whether the complex alters the three dimensional conformation of the low density lipoprotein such that the binding of the low density lipoprotein to a low density lipoprotein receptor is enhanced.
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9. (Three times amended) A method to determine if a compound causes a change in the structure of apolipoprotein B-100 in a cholesterol-containing low density lipoprotein thus increasing the binding of an epitope on the apolipoprotein B-100 to an LDL-receptor, comprising:

- (i) mixing the compound with and allowing it to bind to cholesterol-containing low density lipoprotein forming a complex;
- (ii) exposing the complex to a first capture antibody that is attached to a solid phase material and is directed to the epitope on apolipoprotein B-100 that binds to the LDL-receptor, forming a combination;
- (iii) using a second antibody which binds to the combination;
- (iv) detecting the second antibody bound to the combination by the addition of a third antibody to which is attached a label;
- (v) quantifying the amount of the captured complex by quantifying the amount of label ; and

(vi) comparing the amount of cholesterol-containing low density lipoprotein captured by the assay to a control, wherein an increase in the amount of cholesterol-containing low density lipoprotein captured indicates an increased binding to the low density lipoprotein receptor..

*Depend.*

10. (Twice amended) The method of claim 6, wherein the conformational change in the low density lipoprotein is assessed by observing a change in the electrophoretic mobility pattern of the the low density lipoprotein using electrophoresis.

15. (Three times amended) A method for assessing whether a compound first binds to a cholesterol-containing lipoprotein, enhancing the binding of the cholesterol-containing lipoprotein to a low density lipoprotein hepatic receptor and thus lowering plasma cholesterol, the method comprising:

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(a) allowing the compound to form a complex with a cholesterol-containing lipoprotein in vivo,

(b) isolating the resulting complex, and

(c) determining whether the formation of the complex causes a change in the three dimensional conformation of apoB-100 in the cholesterol-containing lipoprotein that enhances the binding of the lipoprotein to the LDL hepatic receptor.

*D5*

23. (Twice amended) The method of claim 6, wherein the low density lipoprotein is VLDL.

D<sup>6</sup> 29. (Twice amended) The method of claim 9, wherein the control is low density lipoprotein in the absence of test compound.

35. (Amended) The method of claim 15, wherein the cholesterol-containing low-density lipoprotein is LDL.

D<sup>7</sup> 36. (Amended) The method of claim 15, wherein the cholesterol-containing low-density lipoprotein is VLDL.

Please add the following new claims:

37: (new) A method for assessing whether a compound enhances the uptake and clearance of a cholesterol-containing low density lipoprotein comprising:

- D<sup>8</sup> cont'd.
- i) allowing the compound to form a complex with a labeled cholesterol-containing lipoprotein;
  - ii) isolating the complex;
  - iii) allowing the complex to incubate with a cell culture;
  - iv) measuring the uptake of the labeled cholesterol containing lipoprotein into the cells.

38. (new) The method of claim 37, wherein the cell culture is composed of hepatic cells.

39. (new) The method of claim 37, wherein the uptake of labeled cholesterol containing lipoprotein is determined in the presence of an excess amount of unlabeled cholesterol-containing lipoprotein.

40. (new) A method to determine if a compound causes a change in the structure of apolipoprotein B-100 in a cholesterol-containing low density lipoprotein thus increasing the binding of an epitope on the apolipoprotein B-100 to an LDL-receptor, comprising:

(i) mixing the compound with and allowing it to bind to cholesterol-containing low density lipoprotein forming a complex;

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(ii) exposing the complex to a first capture antibody that is attached to a solid phase material and is directed to the epitope on apolipoprotein B-100 that binds to the LDL-receptor, forming a combination;

(iii) detecting the combination by the addition of a second antibody to which is attached a label;

(iv) quantifying the amount of the captured complex by quantifying the amount of label ; and

(v) comparing the amount of cholesterol-containing low density lipoprotein captured by the assay to a control, wherein an increase in the amount of cholesterol-containing

low density lipoprotein captured indicates an increased binding to the low density lipoprotein receptor..

41. (new) The method of claim 40, wherein the control is low density lipoprotein in the absence of test compound.

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